

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings of claims in the application:

Listing of Claims:

1-106. (Canceled)

107. (Currently Amended) A method for determining a methylation profile of a cell, tissue or organism, the method comprising the steps of:

a. providing a population of randomly cleaved or sheared DNA fragments from the cell, tissue, or organism, wherein the DNA comprises a first portion and a second portion and each portion comprises methylated and unmethylated fragments;

b. depleting methylated or unmethylated DNA from the second portion
~~reducing the percent of unmethylated fragments of interest to no more than 40% of the original percent in the population or reducing the percent of methylated fragments of interest to no more than 40% of the original percent in the population;~~ and

c. quantifying the relative amount of at least one sequence from at least two of the following:

the first portion,

methylated DNA in the second portion, and

unmethylated DNA in the second portion

~~quantifying the amount of at least one DNA sequence from step (b) to determine the methylation profile of at least one nucleic acid sequence from the cell, tissue or organism.~~

108. (Canceled)

109. (Canceled)

110. (Original) The method of claim 107, wherein the quantifying step comprises quantitative amplification.

111. (Original) The method of claim 107, wherein the average size of the DNA fragments is between 0.1-10 kb.

112. (Canceled)

113. (Canceled)

114. (Canceled)

115. (Canceled)

116. (Currently Amended) The method of claim 107 ~~115~~, wherein the depleting step comprises:

fragmenting the second portion with a methylation-sensitive restriction enzyme or a methylation-dependent restriction enzyme to produce digested DNA and undigested DNA; and separating the digested DNA from the undigested DNA.

117. The method of claim 116, further comprising:

labeling the first portion with a label;

labeling the digested or undigested DNA from the second portion with a label;

hybridizing the labeled DNA from the first and second portions to a nucleic acid;

and

determining the relative methylation of a nucleic acid by detecting the first and second labels hybridizing to the nucleic acid, thereby determining the methylation profile of at least one nucleic acid sequence from the cell, tissue, or organism.

118. (Currently Amended) The method of claim 107 ~~112~~, wherein the methylated DNA is depleted from the randomly cleaved or sheared DNA.

119. (Currently Amended) The method of claim 107 ~~112~~, wherein the unmethylated DNA is depleted from the randomly cleaved or sheared DNA.

120. (Currently Amended) The method of claim 107, wherein the quantification step comprises hybridizing the DNA ~~depleted~~ ~~reduced~~ of methylated DNA or the DNA depleted of unmethylated DNA to a nucleic acid linked to a solid support.

121. (Original) The method of claim 120, wherein the solid support is selected from the group consisting of a microarray, a bead and a matrix.

122. (Original) The method of claim 107, wherein the organism is selected from a plant, an animal, a fungus, and a prokaryote.

123. (Original) The method of claim 107, wherein the method further comprises comparing the methylation profile of a nucleic acid with a transcription profile of the nucleic acid, thereby determining the relation between methylation profile and the transcription profile of the nucleic acid.

124. (Original) The method of claim 123, wherein the transcription profile of the nucleic acid is detected with a microarray.

125. (Original) The method of claim 107, wherein the method further comprises comparing the methylation profile of a nucleic acid with a chromatin packaging state profile of the nucleic acid, thereby determining the relation between methylation profile and the chromatin packaging state profile of the nucleic acid.

126. (Original) The method of claim 107, further comprising comparing the methylation profile of a specimen of a bacterial pathogen with a reference strain of the pathogen, wherein similarity of the methylation patterns indicates common origin of the specimen and the reference strain.

127. (Original) The method of claim 107, further comprising comparing the methylation profile of the nucleic acid with the copy number of the nucleic acid, thereby determining the contribution to a phenotype of the combination of the methylation of the nucleic acid and the copy number of the nucleic acid.

128. (Original) The method of claim 127, wherein the copy number of the nucleic acid is detected with a microarray.

129. (Original) The method of claim 107, wherein:
the methylation profile of at least a first and a second DNA sample is compared,
step a comprises providing a population of randomly cleaved or sheared DNA fragments from the DNA samples;
step b comprises:

(i) depleting methylated or unmethylated DNA from the randomly cleaved or sheared DNA of the first DNA sample, and

(ii) optionally depleting methylated or unmethylated DNA from the cleaved or sheared DNA of the second DNA sample; and

the method further comprises:

c. comparing the amount of at least one sequence from the depleted first DNA sample with the amount of the sequence in the cleaved or sheared second DNA sample or the depleted second DNA sample.

130. (Original) The method of claim 129, wherein the samples each comprise a first portion and a second portion and the second portion from each sample is depleted for methylated or unmethylated DNA fragments; and

the first portion from the first sample, the second portion from the first sample, the first portion from the second sample and the second portion from the second sample are each labeled and hybridized to a nucleic acid, wherein the ratio of the hybridization of the first portions provides a CGH profile and the ratio of the hybridization of the first and second portions for each sample provides a methylation profile for each sample.

131. (Original) The method of claim 129, wherein the samples each comprise a first portion and a second portion and the second portion from each sample is depleted for methylated or unmethylated DNA fragments; and

two portions are labeled and hybridized to a nucleic acid, wherein the two portions are either:

the first portion from the first sample and the second portion from the first;
the second portion from the first sample and the first portion from the second sample;
the first portion from the second sample and the second portion from the second sample; or
the second portion of the second sample and the first portion of the first sample.

132. (Original) The method of claim 129, wherein the depleting step comprises:
digesting the randomly cleaved or sheared DNA with a methylation-sensitive or methylation-dependent restriction enzyme to produce DNA digested by the restriction enzyme and DNA undigested by the restriction enzyme; and
separating the digested DNA from the undigested DNA.

133. (Original) The method of claim 132, further comprising:
labeling the digested or undigested DNA with a label;
hybridizing the labeled DNA to a nucleic acid; and
determining the methylation state of at least one nucleic acid sequence by detecting the labeled DNA hybridizing to the nucleic acid.

134. (Canceled)

135. (Canceled)

136. (Canceled)

137. (Canceled)